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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/641,801	08/17/2000	G. John Stanton	265.0023 0101	5388

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EXAMINER
NICHOLS, CHRISTOPHER J

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 09/04/2002 CO

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/641,801	Applicant(s) STANTON ET AL.	
	Examiner Christopher J. Nichols	Art Unit 1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 July 2002*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-36* is/are pending in the application.

4a) Of the above claim(s) *36* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-35* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-36* are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *5,6*.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Election/Restriction

1. Applicant's election with traverse of Group 1 (Claims 1-35), in part drawn to methods of contacting cells with SEQ ID NO: 1 in Paper No. 8 (17 July 2002) is acknowledged. The traversal is on the ground(s) that examination of Group 35 would not be a burden and that of the 69 groups would require substantial duplication of work on the part of the USPTO. Applicant further argues that the 69-way restriction is a burden for Applicant in terms of filing and maintenance fees. Finally, Applicant argues that Claim 29 is a linking claim and the restriction should have been a requirement to elect a species. Applicant's arguments have been fully considered but are not found to be persuasive. This is not found persuasive because, with regard to Group 35, examination of specific combinations of peptides requires a significant extension of the search required for the elected peptide. It is noted that the claims recite open claims language. Therefore, the elected invention is drawn to methods comprising contacting cells with SEQ ID NO: 1, and the claims embrace methods wherein cells are contacted with generic compositions comprising SEQ ID NO: 1. While the cost to applicant is regretted, the search required for any one peptide recited in the claims is non-coextensive with the search required for any other. Each peptide requires a unique search of the sequence and literature databases. Therefore, an undue search burden is required of the examiner to search all of the peptides together. Finally, regarding Claim 29, it appears that Claim 29 is not a linking claim, since the generic "constituent peptide thereof" does not accurately reflect the Markush group recited in Claim 1, for example. The specifically recited peptides are a subgenus. Since each peptide is structurally unique, restriction was proper. Claim 36 is withdrawn from further consideration pursuant to 37 CFR

1.142(b), as being drawn to a nonelected material, there being no allowable generic or linking claim. Claims 1-35 will be examined to the extent that they read on methods of administering SEQ ID NO: 1, active analogs thereof, and generic compositions comprising the peptide SEQ ID NO: 1.

Status of Application, Amendments, and/or Claims

2. The preliminary amendment of 18 June 2001 (Paper No. 5) has been entered in full. The sequence listing has been found to be free of errors and has been entered into the file. Claim 36 is withdrawn from consideration, as discussed above. Claims 1-35 are under examination.

3. The Art Unit location of your application in the USPTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Art Unit 1647, Examiner Christopher Nichols.

Specification

4. The Specification is objected to because of the following informalities: spelling error, "downstream" (pp. 7 line 19). Appropriate correction is required.

5. The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

Claim Objections

6. Claims 1-35 are objected to because of the following informalities: the claims recite non-elected inventions. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 1-35 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods of inducing a cytokine in a cell, or modulating an immune response in a cell or patient, or modulating peripheral blood leukocytes, comprising administering the peptide of SEQ ID NO: 1 or one active analog thereof which is full-length colostronin, does not reasonably provide enablement for the claimed methods wherein any blood cell is modulated, or analogs other than full-length colostronin is administered. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims. Claims 1-5 are directed to methods of inducing a cytokine in a cell comprising administering SEQ ID NO: 1 or an active analog thereof. Claims 6-19 are directed to methods of modulating immune response comprising administering SEQ ID NO: 1 or an active analog thereof. Claims 20-34 are directed to methods of modulating blood cell proliferation comprising administering SEQ ID NO: 1 or an active analog thereof. The specification teaches that full-length colostronin and the peptide SEQ ID NO: 1 has diverse effects when administered to cells or organisms. Specifically, the specification discloses that colostronin and SEQ ID NO: 1 stimulates peripheral blood leukocytes

in culture. The specification also discloses that colostronin and SEQ ID NO: 1 stimulates secretion of several cytokines including IFN-γ, IL-10, and IL-6. The prior art teaches that colostronin is a polypeptide found in colostrums (Janusz et al. WO 98/14473). The isolated, full-length colostronin is disclosed as exhibiting a capacity to stimulate the growth, maturation, and differentiation of immunologically active cells when administered to both humans and in experimental animals. Janusz et al. also teaches that in cultures of lymphocytes of human peripheral blood colostrinin is characterized in that it stimulates the production of cytokines, especially IFN-γ, TNF-α, interleukins (e.g. IL-6 and IL-10) and various growth factors (see pp. 8 lines 1-11). The scope of patent protection sought by Applicant as defined by the claims fails to correlate reasonably with the scope of enabling disclosure provided by the specification and prior art for the following reasons.

8. Regarding analogs, the art recognizes that even minor alterations to protein structure have unpredictable effects on a proteins function. Due to the large quantity of experimentation necessary to all the applicable analogs of SEQ ID NO: 1, the lack of direction/guidance presented in the specification regarding synthesizing, screening, and evaluating non-peptide analogs of SEQ ID NO: 1, the absence of working examples directed to non-peptide analogs of SEQ ID NO: 1, the complex nature of the invention, the unpredictability of the effects of mutation on protein structure and function (see Ngo et al. (1994) and Wells (1990)), and the breadth of the claims which fail to recite limitations for what constitutes an analog, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

9. Regarding the scope of blood cell proliferation, the art recognizes the enormous range of blood cells and their corresponding regulators and modulators. Due to the large quantity of experimentation necessary to evaluate the effects of SEQ ID NO: 1 on all blood cells, the lack of direction/guidance presented in the specification regarding study of SEQ ID NO: 1's effect on all blood cells, the absence of working examples directed to non-peripheral blood leukocyte blood cells, the complex nature of the invention, the unpredictability of effects any new peptide would have on any blood cells (see Elgert "Immunology"), and the breadth of the claims which fail to recite limitations which blood cells, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) do not apply to the examination of this application as the application being examined was not (1) filed on or after November 29, 2000, or (2) voluntarily published under 35 U.S.C. 122(b). Therefore, this application is examined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

10. Claims 1-10 are rejected under 35 U.S.C. 102(b) as being anticipated by Inglot et al. (1996) Archivum Immunologiae et Therapiae Experimentalis (44) 215-224. Inglot et al. (1996) teaches a method of inducing a cytokine in a cell, comprising administering full-length colostronin, which meets the limitations of an "active analog" of SEQ ID NO: 1 in Claims 1-10 (pp. 215). Inglot et al. (1996) teaches a method of using colostrinin (or colostrinine or PRP) and a constituent peptide fragment thereof (NP: VQSYVPLWP) as pleiotropic immunological

regulators to induce cytokines, such as IFN-γ and TNF-α, in mammalian cells (*in vitro*) and as being administered to mice (*in vivo*) and humans thus meeting the limitations of Claims 1-5 (Introduction pp. 216, Materials and Methods pp.216, Tables 1-4). Regarding Claims 1-5 Inglot et al. teaches the method wherein the cell is presented in a human organism, thus meeting the limitations of Claims 2-4. So, Inglot et al. anticipates Claims 1-5. Furthermore, Inglot et al. (1996) teaches that colostronin (PRP) is active as an immunostimulant in regards to modulating immune responses including inducing cytokines in cells, mice, and humans (pp. 215). Therefore, Inglot et al. (1996) anticipates Claims 1-10.

11. Claims 11-19 are rejected under 35 U.S.C. 102(b) as being anticipated by Janusz et al. (WO 98/14473). Janusz et al. (WO 98/14473) teaches a method directed to modulating an immune response in a patient, comprising administering an immunological regulator, in this case full-length colostronin, which meets the limitations of an "active analog" of SEQ ID NO: 1 in Claims 11-19 (pp. 10 lines 5-19). Regarding Claims, 11-19, Janusz et al. (WO 98/14473) teaches that colostronin (PRP) can be administered to animals, including humans, via a dietary supplement or topically thus meeting the limitations of Claims 13-16 (pp. 2 lines 2-5; pp. 3 lines 1-10, 23-30; pp. 4 lines 1-5; pp. 6 lines 17-30; pp. 7 lines 1-13; pp. 8 lines 27-30; pp. 9 lines 1-260). Regarding Claims 11-19, Janusz et al. (WO 98/14473) teaches that colostronin (PRP) when administered to animals, including humans, can elicit a specific or nonspecific (i.e. humoral or cellular) immune response, including antibody production, and trigger IFN-γ response thus meeting the limitations of Claims 17-19 (pp. 2 lines 29-30; pp. 3 lines 1-11; pp. 7 lines 23-30, pp. 8 lines 1-11; pp. 9 lines 1-16). Therefore, Janusz et al. (WO 98/14473) anticipates Claims 11-19.

12. Claim 20-35 are rejected under 35 U.S.C. 102(b) as being anticipated by Janusz et al. (WO 98/1443). Janusz et al. (WO 98/14473) teaches a method comprising administering full-length colostronin, which meets the limitations of an "active analog" of SEQ ID NO: 1 in Claims 26-28 and 33-35 (pp. 4-6). Furthermore Janusz et al. (WO 98/14473) teaches a method of using colostronin as a dietary supplement for adults who have been subjected to chemotherapy or improving the development of the immune system of a new born child, hence modulating blood cell differentiation and proliferation thus meeting the limitations of Claims 20-25 and 29-32 (pp. 3 lines 15-30; pp. 4 lines 1-10). In addition, Janusz et al. (WO 98/14473) teaches that colostronin is characterized by immunotropic action, both in vivo and in vitro, based on the properties of modulation, differentiation, and maturation of thymocytes to active T cells thus meeting the limitations of Claims 21, 24-25, and 31-32 (pp. 7 lines 23-30; pp. 8 lines 1-11). Also, Janusz et al teaches that colostrinin can be used to greatly accelerate the maturation of stem cells, which are capable of reproduction of hematopoietic cells and of various immunologically-active blood cells thus meeting the limitations of Claims 21, 24-25, and 32-32 (pp. 19 lines 30-40). Therefore, Janusz et al. (WO 98/14473) anticipates Claims 20-35.

Conclusion

13. Claims 1-35 are hereby rejected.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christopher Nichols, PhD whose telephone number is 703-305-3955. The examiner can normally be reached on Monday through Friday, 8:30AM to 5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz, PhD can be reached on 703-308-4623. The fax phone numbers for the

organization where this application or proceeding is assigned are 703-872-9306 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Elizabeth C. Kemmerer

CJN
August 19, 2002

ELIZABETH KEMMERER
PRIMARY EXAMINER